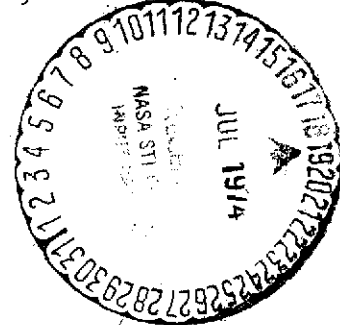# THE BIOPHYSICS OF STRONG INTERACTIONS OF HIGH ENERGY HADRONS

I. G. Akoyev and S. S. Yurov

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16. Abstract

The authors discuss the effect of high and super high energy hadrons on the functions and genetic structures of different organisms. The authors use materials from studies performed on a 70 GeV proton accelerator, using a source of gamma radiation and material from various Soviet and American space studies. Although the research conducted shows that the effect of the strong interactions of high energy hadrons can cause significant damage to cellular and genetic structures, radiation-protective measures may prove to be effective.

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Results of experimental-analytical investigations on the biophysics of high energy hadrons are given. The genetic and somatic effects obtained in experiments on an accelerator and in space are examined in connection with the characteristics of strong nuclear interactions.

The prospects of hadron biology are discussed.

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THE BIOPHYSICS OF STRONG INTERACTIONS OF HIGH ENERGY ADRONS

I. G. Akoyev and S. S. Yurov

INTRODUCTION

In connection with the successes of atomic science and tech- /3*
nology, an ever greater number of people are working in institutions
and industries where high and super high-energy radiation is used.
Providing for their safety requires particular attention to be
given to the sanitary-hygienic rating of human stays
in zones which may be affected by nuclear particles and radiation.

The entry of man into outer space has required great
attention to be given to problems of the biological effect of cos-
mic radiation and its superhard components. Without studying them
it is impossible to solve the problem of providing safety on a
long space flight either on continously operating orbital stations
or in flights to other planets.

In solving the problems imposed by sanitary-hygienic
rating and determining the danger of the effect of ionizing radia-
tion, as is known, it is necessary to proceed from the character-
istics of the biological effects of a given type of radiation and
the laws of determining an effective dose [1, 9, 10]. The bio-
logical effects of radiation of "normal" energy have been studied
for a long time. However, for nuclear corpuscular radiation of
high energies, the biological effects have still not been suffi-
ciently studied, and for radiation with an energy of several tens
of giga-electron volts the biological effects are simply unknown.
Theoretical predictions of the biological effect of nuclear radia-
tion of high energies, as will follow from the discussion below,
are not confirmed. For this reason even the quantitative para-
meters of the formation of an effective dose are also not clear.

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*Numbers in the margin indicate pagination in the foreign text.

The startup of the Serpukhov proton accelerator of the Institute of High Energy Physics has for the first time made it possible to obtain nuclear corpuscular radiation of super-high energies up to 70 giga-electron volts. The so-called strong hadron interactions are already characteristic for such radiation. As opposed to other results of interaction (electromagnetic and elastic nuclear) in the case of the interaction of super high energy hadrons, there takes place a nuclear decay into mesons and other nucleon fragments. For this reason, as a result of one such strong interaction, up to several dozen, and sometimes hundreds of secondary particles may be formed, part of them, in turn, capable of causing a similar process with subsequent strong interactions. A result of strong interaction may also be the birth of heavy particles and anti-particles (for example, anti-protons). In connection with the high energy and speed of the hadron a flux of secondary particles is characterized by a narrow angular distribution and extreme irregularity in the local density of the energy absorbed by a biosubstrate [14, 15]. The biological effect of such processes is completely unstudied. Essentially, radio biology and radiation medicine never previously had to deal with these processes and therefore they are still not prepared for experimentally well-founded evaluation of the possible biological consequences of the effects of super hard radiation. The total effect of these circumstances has been to /4 require that special experiments be set up with the aim of studying the biological effect of strong interactions of hadrons of high and super-high energies.

The goal of the present study was to evaluate the biological effect of the secondary radiation generated on a target by protons with an energy of 70 giga-electron volts, according to their effect on objects which may be studied in the given conditions. These, first of all, are vegetable objects: horse bean seeds (physiological and cytogenic factors); virus and microbiological objects; bacteria (survival) and bacteriophages (survival) and mutagenesis with subsequent genetic analysis. In addition, research on

mammalian cells with respect to the influence of radiation on the
gonads was begun and conducted. The research with respect to the
development and experimental verification of methods of dosimetric
control of irradiated objects was very complex and laborious.[1] The
development and perfection of dosimetry methods was conducted in
parallel with experiments on biological objects, therefore in the
course of the investigation corrections were introduced into the
results of the first experiment taking account of the new dosimetry
data.[2]

In the investigations conducted the biological effects of radiation of such high energy was studied first. It has been established that with respect to somatic and genetic effects this radiation may be significantly more dangerous than was expected. This
did not correspond with the traditional concept of a rigid connection between mean linear energy transmissions and the relative biological effect of radiation, which forced us to turn particular attention to the problems of the biophysics of the strong interaction
of high energy adrons as they are understood by biologists.

THE BIOPHYSICAL CHARACTERISTICS OF THE INTERACTION OF HIGH ENERGY ADRONS

An analysis of the contemporary state of the question of the
influence of strong nuclear interactions on biological elements
showed that this new direction in radiobiology, which may be
called hadron biology, has great theoretical and practical significance.

The interactions of negative pions of comparatively low energies with light atoms have been studied the most [Fowler, Mays,

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[1] The research was conducted by our colleagues at the Institute of
High Energy Physics, V. N. Lebedev and V. S. Lukanin.

[2] These problems have also the physical characteristics of strong
interactions of high-energy hadrons and will be examined in more
detail in a special preprint from the Institute of High Energy
Physics.

1967; Baarli, 1971, Kartis, 1971]. Negative pions even at low energies are capable of causing splitting of the nuclei of light elements with the formation of "stars" from the fragments of the nucleus (Fig. 1), and the conversion of one element into another. For example, upon the reaction of such a pion with oxygen it is possible to have the formation of eight isotopes of six new chemical elements. Here the energy of the "stars" is absorbed in a comparatively small volume. In secondary electromagnetic action, a significant role may be played by heavy nuclei possessing high biological effectiveness. A number of unusual reactions may also take place simultaneously with the conversion of nuclei into other elements. The replacement of an electron from the inner shell of an atom by a minus-π-meson or minus-μ-meson with the formation of mesonic atoms (meso atoms) is possible.
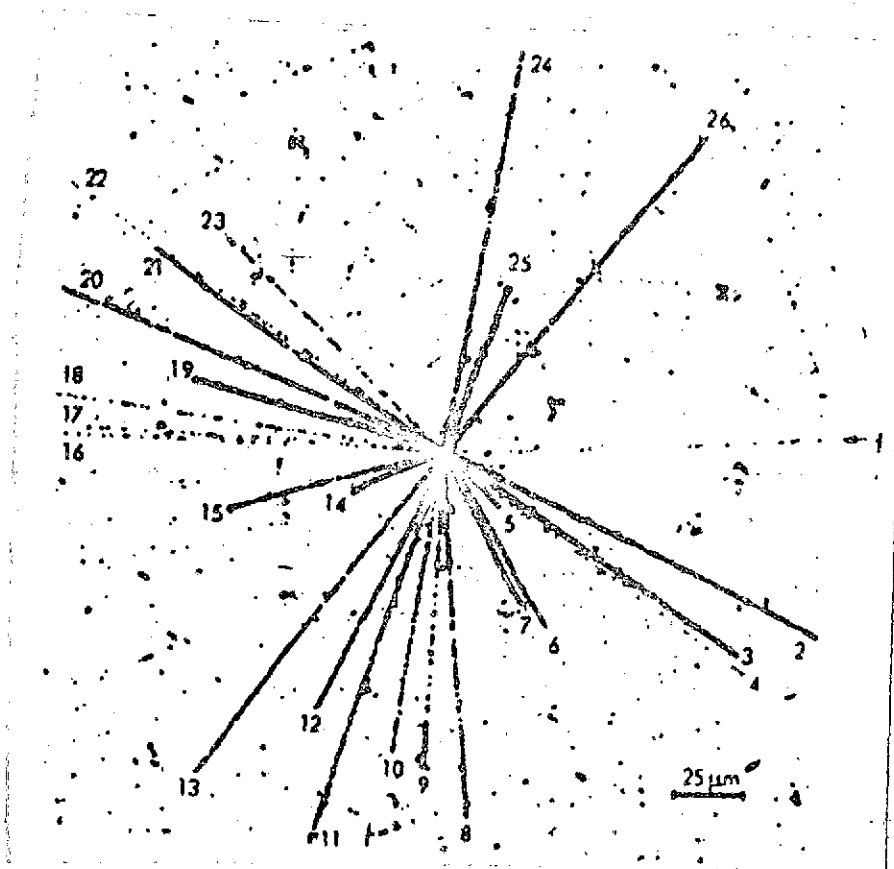

Figure 1. Typical picture of the formation of a "star" as the result of the collision of a π-meson with the nucleus of an atom of a photographic emulsion (Kleyfosh).

The physical-chemical characteristics of such unusual states of
elements has still not been completely studied. It has been
established that the oxygen nucleus in oxides intercepts mesons
with a higher probability than do other chemical nuclei. Large
mesomolecules are formed in these reactions. Mesoatoms may par-
ticipate in charge exchange reactions (in the case of low collision
energies with the formation of unstable chemical compounds) and
substitutions (with the formation of more stable mesomolecules).
Further, mesoatoms which have been formed either split nuclei, or
produce nuclear transformation with the emission of protons, deutrons and
tritons.

Thus, in the example of the capture of stopped negative
pions of comparatively low energy by nuclei of light elements
we see a basically new type of radiation effect, relating to
strong interactions.

Let us now consider the possible characteristic reactions
of super high energy adrons with matter [Dobrotin, 1954; Zhdanov,
1964; Schein et al, 1960; Boykher et al, 1960; Akashi, 1968;
Peters, 1960, 1964; also 2, 14, and 15]. Unfortunately, detailed
information of the interactions of high and super-high energy adrons
does not exist. However, there are data which point to the
basically important characteristics of their interaction. Analysis
of the experimental material shows that one of the principal characteristic
consequences of their strong interaction is the formation not of
"stars" but of a narrow beam of high energy secondary particles.
It is also necessary to emphasize the not insignificant character-
istic feature of the narrow beam of high energy secondary particles
formed: the presence of hadrons among them and, consequently, the
possibility of the secondary formation of strong interactions and
narrow beams of new secondary particles. There are also among
them heavy nucleii and antiprotons. The antiprotons may, in
turn, give birth to π-minus-mesons.

The research conducted in the Institute of High Energy Physics on the Serpukhov accelerator with proton energies up to 70 giga-eV made it possible to get a good idea of the above mentioned characteristics of the interaction of high and super-high energy adrons. Figure 2 shows a reduced photograph of the multiple generation of secondary nuclear particles as a result of strong interaction of one pion with an energy of 47 giga-eV with one carbon nucleus of a propane chamber (1). The small angle of distribution of the secondary charged particle tracks is clearly seen (2, 6). The tracks of heavy nucleii are visible (3). As a result of subsequent strong interactions (4 and 7) some secondary adrons form a great number of new nuclear particles, including heavy ions (5) for which a small angle of distribution is also characteristic. The extreme irregularity of the local distribution of absorbed energy is graphically seen. Such a high multiplicity of second particle generation, equal to 63 for charged particles in the given example, is not completely characteristic. More often less than 15 secondary particles are generated with a narrow angular distribution depending on the energy that is, the velocity, of the primary article.

Consequently, a very high multiplicity of secondary-particle generation aandt the presence among them of heavy nucleii or slowed π-minus mesons is a comparatively rare phenomenon having a statistical nature.

It is also necessary to note one more characteristic of strong interactions of high and super-high energy hadrons: the latter may enter into nuclear reactions wth practically any atom of molecules, since in the case of such high energies there are no interaction resonance peaks. Consequently, the molecules may be at other than just the points with the least solid chemical bonds.

Finally, at the high and super-high energies under consideration

the nature of the nuclear particle, hadron (its type, weight and charge), evidently, may no longer play a significant role. For example, at energies below 100 mega-electron volts, of all mesons only charged mesons are hadrons, that is, particles capable of strong interaction. In addition, the ability to form "stars" is greater in the case of a negative π-meson than in the case of a positive one. However, at energies exceeding several dozen giga-eV, all the types of negative, neutral and positive mesons (except for muons), and also protons and neutrons become hadrons. The probability of nuclear interaction depends basically only on the distributional density of atomic nuclei, and the result of interaction is the same.

The above-mentioned physical characteristics of the interaction of high and super-high energy adrons with matter force us to assume a number of biophysical differences in their biological effects. This emphasizes the basic novelty of hadron biology and the importance of studying the biological effects of hadrons from the theoretical and practical points of view.

EXPERIMENT AND ANALYSIS

In order to study the biological effects of high energy hadrons we used both our own experimental investigations and the Protvino accelerator of the Institute of High Energy Physics [2-8, 12-15] and also the results of an analysis which we made of biological experiments in space [2, 14, 15] performed by Soviet and American investigators.

Results of Accelerator Investigations

Biological investigations were conducted in the field of influence of secondary emissions from protons of 70 giga-eV, generated on a target. The region for irradiating biological objects on the accelerator was chosen on the basis of the desire to obtain as high a dosage as possible with the maximum

contribution of uncharged high energy hadrons to the total particle flux. The region of the target in which is singleddout the line corresponding to the zero angle of escape of hadrons from the target ("zero line") corresponds to these requirements to the greatest degree. Biological objects were placed along it at an equal distance from the target in such a way as to provide for the necessary variations in dose during simultaneous irradiation. Est- /8 imated calculations showed that high energy hadrons in the chosen region are the basic component of the radiation field. Their mean spectral energy lies in the range between 10 and 40 giga-eV; pions, 3.5 giga-eV). In addition to high energy hadrons at the irradiated point there are neutrons with an energy less than 20 mega-eV, leptons and photons [15]. Unique activation detectors are placed with each biological object, and a tissue-equivalent ionization chamber was located at one of the points on the "zero line."

Physiological Indicators Vicias faba[3]

All experiments on V. faba were made together with Fomenko, Akhmadiyeva and Livanova [3, 5, 12-15]. Seeds having a moisture content of $8.55 \pm 0.19\%$ were irradiated in organic glass cups 30 mm in diameter and 80 mm in height with a wall thickness of 2 mm. The cups were attached along the zero line. A gamma ray source with a dosage of 441 rad/min served as the source of the control Cs^{137} gamma radiation. The deviation in irradiating the seeds on the gamma-source was not more than 12 hours in comparison with irradiation on the accelerator. In all, three parallel experiments were performed, and in addition, three supplementary experiments were performed with irradiation on the gamma radiation source. The results of all experiments were generalized by single approximating curves.

Three days after irradiation, the seeds were soaked for 24 hours at a temperature of 25°C. After this the seed coats were

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[3]This and the following sections were written together with B. S. Fomenko.

Figure 2.   Results of the interaction of one pion with an energy of 47 giga-eV with a carbon nucleus in the propane chamber of the Institute of High Energy Physics. The length of the photograph region is around 2 meters [8].

removed and they were grown on Petrie dishes in a thermostat at the same temperature. Four day shoots, grown in the thermostat, were transferred into a water culture and then grown to an age of 12 days in conditions of natural illumination at a temperature of 23-25°C. The daily growth of the primary root was measured from the fourth day growth. The survival and the dry weight of the plants was considered on the twelfth day growth.

Averaged data on the death of primary roots to the 12th day after beginning of soaking the seeds in relation to the dose of their irradiation showed that dose-effect curves (Ordinate in test units) with the irradiation of seeds on the accelerator satisfied in equation $y = 1.42 \bar{\bar{x}} + 1.71$ and with Cs^{137} gamma radiation $y = 0.61 \bar{\bar{x}} + 1.98$. The dose ($\bar{\bar{x}}$) here and below is kilorads. Semilethal doses calculated on the basis of these equations had values of, respectively, 2.70 and 4.95 krad, and their ratio was 1.9.

The relationships between the decrease in the dry weight of 12 day plants and the dose had the form of $y = 0.17 \bar{\bar{x}} + 2.23$ in the case of gamma irradiation and $y = 0.30 \bar{\bar{x}} + 2.29$ in the case of irradiation of the accelerator, and the doses of half suppression of plant weight – 3.09 and 1.93 krad, respectively. The effectiveness of the secondary accelerator radiation according to the given criterion exceeded the effectiveness of the Cs^{137} gamma radiation by 1.6 times. In the case of high doses (above 5.5 krad gamma radiation and 3.5 krad secondary accelerator radiation) the straight line nature of the dose relationship was destroyed.

Similar data are also obtained in experiments in which the effective radiation of the length of the primary root served as the criterion of damage. Root growth in length, as also plant weight, were somewhat stimulated by small doses of radiation. Beginning with a gamma radiation dose of 1.8 krad and an accelerator radiation dose of 1.0 krad suppression of root growth in length

is proportional to the dose. With doses above 5.5 krad for gamma radiation and 3.8 krad in the case of accelerator radiation a deviation from proportionality was observed which results from the higher radiation resistance of the process of the extension of the embryonic root. The dose curve for 9 day plants with gamma irradiation satisfied the equation $y = -0.16\bar{\bar{x}} + 2.26$ (ordinate logarithm of the percent of suppression of growth in length) and for 12 day plants $y = 0.19 \bar{\bar{x}} + 2.39$. The equations of the same curve in the case of the irradiation of seeds on the accelerator had the form $y = 0.20 \bar{\bar{x}} + 2.11$ and $y = -0.23 \bar{\bar{x}} + 2.20$, and for the 9 and 12 day plants respectively. The doses for half suppression of the growth in length of the primary root for the 9 and 12 day plants in the case of gamma irradiation were 3.42 and 3.59 krad and in the case of irradiation on the accelerator, 2.06 and 2.16 respectively. The coefficients of biological effectiveness of secondary accelerator radiation, calculated from the half suppression of root growth doses, are 1.66 for the 9 day plants and 1.60 for the 12 day plants.

Measurement of the daily growth of the primary root from the 4th to the 12th day of vegetation showed that it somewhat increased with time during the experiment, while in the control the growth rate during the experiment remained almost constant. The total data of six experiments were averaged with respect to the daily increase in root length of the plants grown from the gamma irradiated seeds, expressed in fractions of the daily growth with respect to the control. The degree of increase in daily growth from the time after the beginning of wetting the seeds depended on the dose; with one and the same dose the daily growth during the experiment is satisfactorily described by first order equations. For the different doses of gamma radiation these had the form for 0.46 krad - $y = 0.003 t + 1.11$; 0.92 krad - $y = -0.0092t + 0.88$; 1.84 krad - $y = -0.0251t + 0.64$; 2.76 krad - $y = -0.0471t + 0.23$; 3.68 krad - $y = 0.0547t + 0.0381$; 4.60 krad - $y = 0.0262t + 0.0222$, where t is

the age of the plants in days.

An analysis of these equations shows that in the case of small doses of gamma irradiation the angle of inclination of the curve increases with an increase in the dose and reached a maximum value at 3.7 krad; in the case of higher doses the angle of inclination decreased. In the case of doses exceeding 4.6 krad and more, the destruction of a significant portion of the plant was observed. A dose of gamma radiation which, as was already noted, was observed to have a tendency to stimulate growth processes, also caused a certain increase in the angle of inclination of the curve, and the free term in the equation exceeded unity.

It is obvious that the angle of inclination of curve of the dependence of relative growth on time in the given case may serve as an approximate characterization of the rate of recovery of root growth. The relative rate of recovery of growth in the case of gamma irradiation of seeds up to a dose of 3.7 krad inclusively directly depended on the dose. Similar regularities are also noted in the case of the irradiation of seeds by secondary accelerator radiation. In the given case the rate of recovery of growth of the primary root was calculated for each of the doses studied separately. They served as the basis for plotting the curve of the dependence of rate of recovery of root growth on the dose. For a quantitative characterization of the connection between the dosage dependences of the rate of recovery of primary root growth in the case of the types of ionizing radiation studied, the coefficients of their regression lines were used. In the case of the irradiation of seeds with gamma radiation the dosage curve of the rate of recovery followed the equation $K_1 = 0.017x + 0.0067$; in the case of irradiation on the proton accelerator; $K_1 = 0.0315x - 0.0051$. The relative biological effectiveness of secondary radiation in comparison with the effectiveness of CS^{137} gamma radiation (according to the criterion of the degree of activation

of recovery processes was equal to 1.85.

CHROMOSOME DAMAGE IN V. faba

The massive entering of cells into first mitosis was observed 56-60 hours after the beginning of soaking the seeds with a primary root link of 14-15 mm; the first fixation was made at this length. In order to facilitate statistical analysis of the results it is assumed below that the first fixation in all experiments was made at the same time, that is 50 hours after the beginning of soaking the seeds. The subsequent free fixations were made at five hour intervals. Considering that the duration of the mitotic cycle for the primary root of horse bean at the given growing temperature is around 23 hours, all four fixations were made during the first mitosis. In each experiment ten roots were fixed in a mixture of ethanol and acetic acid (3:1). The roots were stained with fuchsin-sulfuric acid and semipermanent specimens prepared on each of which 50 ana-telophases were studied. The number of cells with bridges and fragments, and also the number of fragments and bridges on a cell, were calculated.

The biological effectiveness of secondary proton accelerator /10 radiation was evaluated according to the dosage curve of the number of abnormal mitoses or the number of chromosome damages per cell, obtained in the case of the irradiation of seeds with CS^{137} and on the accelerator.

In the case of a straight line connection in dose-effect curves the relative biological effectivenesses were determined with respect to the angles of inclination of the given curves; in the case of a nonlinear connection the mean values of the relative biological effectiveness were calculated according to the individual values obtained for each of the doses in the case of irradiation on the accelerator.

The cytogenic effects of the radiation were studied on roots in the stage of first mitosis. Beginning with the 56th to 60th hour after the beginning of soaking the seeds, when the length of the primary root reached 14-16 mm, the first fixation was made. The subsequent three fixations were made at five hour intervals. The data obtained on the number of cells with abornal ana-telophases (with bridges and fragments) were used for analyzing the "time-effect" curves for different irradiation doses. The results of the first and third fixations were used for examining the dosage dependence of the number of abnormal mitoses under the influence of both types of radiation.

The dependence of the number of ana-telophases with fragments on the dose of irradiation for the gamma irradiation is plotted on the basis of averaged data of three independent tests. The proportion of cells with fragments increased with increasing dosage. The connection was close to straight-line in nature and was satisfactorily described by the equations $y = 14.98x + 1.08$ in the case of gamma-irradiation and $y = 27.73x + 3.05$ in the case of irradiation of seeds on the accelerator. With respect to the angles of inclination of the dosage curves the effectiveness of accelerator radiation was 1.85.

The nature of the dosage curves changed with time after irradiation (Figure 3).
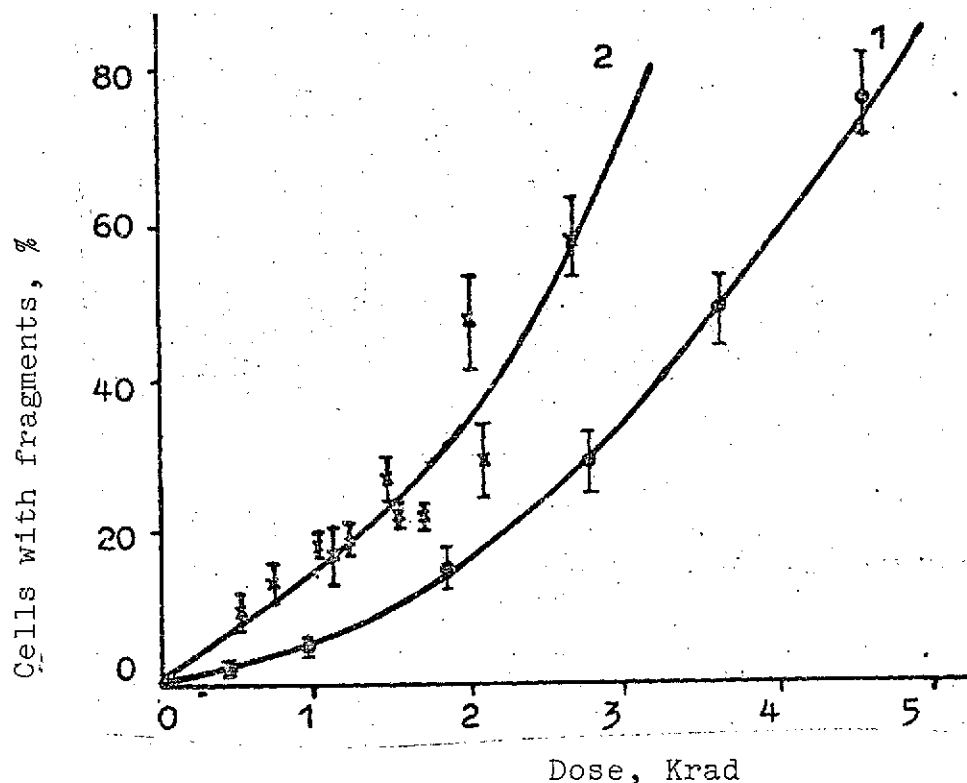
14

Fig. 3.   Number of cells with fragments in the case of
irradiation of seeds with Cs^{137} gamma rays (1)
and accelerator radiation (2).   Third fixation.

In the given case the mathematical description of the dosage curves
of the number of gamma-telophases with fragments is given by a
second-order equation.   The dosage dependence of the number of
cells with fragments in the case of gamma irradiation was described
by the equation $y = 3.07x^2 + 1.49x + 1.62$ and in the case of
accelerator irradiation $y = 2.78x^2 + 10.72x + 1.62$.   The equation   /11
of the "dose-number of cells with fragments" curve, obtained in
the case of the irradiation of seeds with Cs^{137} gamma rays, was
used to calculate the gamma radiation doses corresponding to the
same effect observed in the case of the irradiation of seeds on
the accelerator.   On the basis of the actual doses of accelerator
radiation and the gamma radiation doses corresponding to them in

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effectiveness, we determined the individual, and then the mean values of relative biological effectiveness. The comparative effectiveness of accelerator radiation varied regularly, increasing with an increase in the dose from 1.3-1.4 to 2.4-3.3. Similar results are also obtained with respect to the number of cells with bridges (Table 1). The effectiveness of accelerator radiation with respect to the criterion of the number of cells with bridges exceeded the effectiveness of gamma radiation by 1.9 times.

TABLE 1

EFFECTIVENESS OF ACCELERATOR RADIATION IN COMPARISION WITH Cs^{137} RADIATION WITH RESPECT TO THE NUMBER OF ABERRANT CELLS WITH FRAGMENTS. THIRD FIXATION.

Acclerator radiation dose, krad	Cells with fragments, %	Gamma Radiation corresponding to the same effect	Relative biological effectiveness
0.5	10.00	1.66	3.32
0.7	13.23	1.72	2.45
1.0	17.33	2.03	2.03
1.1	17.64	2.06	1.87
1.2	19.30	2.17	1.80
1.5	27.13	2.76	1.84
1.5	22.0	2.35	1.56
1.7	22.05	2.35	1.40
2.0	46.89	3.60	1.80
2.1	28.81	2.74	1.30
2.7	51.28	3.79	1.40
Mean value			1.88 ± 0.18

The percentage of damaged cells decreased with time after soaking. The rate of decrease depended on the dose and between 460 rad and 3.7 krad increased with increasing dosage; finally, with a dose of 4.6 krad a certain drop in the rate of decrease of ana-telophases with fragments in time was observed. A similar change in the degree of damage during the first mitosis with time and its connection with dosage in the case of irradiation of seeds on the accelerator [13]. The dosage dependence of the rate of decrease

in the number of abnormal ana-telephases in the dosage range 0-3.7·
krad in the case of gamma radiation and 0.21 krad in the case of
irradiation of seeds on the accelerator was close to straight-line
in nature. In the case of higher doses the straight-line nature of
the dosage curves was destroyed. In the dosage range under considera-
tion the curves are described by the equations $y = -0.04 - 0.54x$ --
with respect to the number of cells with fragments, $y = -0.57x + +0.01$ -- with respect to the number of cells with bridges and
fragments in the case of gamma irradiation and $y = -0.97x + 0.18$ and
$y = -0.98x + 0.27$, respectively. Consequently, the dosage dependence
of initial damage (with respect to the free term) and the recovery
rate (with respect to the angle of inclination), calculated from
these equations, represent a value proportional to the dose for
both types of radiation in the given dosage range.

The increasing rate of decrease in the number of cells with
damaged chromosomes and recovery of primary root growth with
increasing dosage, evidently, may be considered from the position of
activation to be proportional to the damage of reparation processes
in this dosage range [1].

The data obtained concerning the effectiveness of accelerator
radiation on plants with respect to all indices studied are given
in Table 2. Data on the number of chromosome fragments and
bridges per aberrant cell are also given there. Upon analyzing
all the results it follows that the accelerator radiation was most
effective with respect to the chromosome fragmentation calculated
per cell (higher probability of multiple damage to cell structures),
and at the same time the least effective with respect
to the degree of activation of recovery processes according to this
same criterion.

SURVIVAL OF BACTERIA AND PHAGES

The experiment we performed on plants revealed a number of
characteristics of the biological effects of high energy adron

radiation, generated on a target by protons of 70 GeV.
Despite the low mean linear energy transmission values the biological
effectiveness proved to be of 1.0, especially with respect to the
number of chromosome fragments in each cell [5]. The latter made
it possible to assume a higher probability of the simultaneous
appearance in each cell of several chromosome injuries. At the same
time recovery processes took place, and the comparative effective-
ness of the action of this radiation significantly increased in
the small dosage range.

That which has been presented above forced us on the next
stage of our research to use objects (bacterial and bacterial phages)
which would allow us to approximate a study of certain molecular
mechanisms of the effect of high energy hadrons.[4]   In the experiments
with E. coli B, E. coli K-12 (λ) we used 6-hour cultures, grown
in nutritive broth.   The bacteria were centrifuged twice and
then twice washed in a buffer, and after this resuspended in a
minimal culture medium (without glucose) to a concentration of
$1 \cdot 10^8$ bacteria per milliliter. The bacterial suspension was pre-
pared 1-2 days before the experiment and the prepared culture
preserved at +4°C. After this the bacteria were placed in 1.5-2 ml
ampules with a wall thickness of 0.2 cm and sealed up on a gas
burner. The irradiation took place at room temperture simultaneously
on the accelerator and on the Cs^{137} gamma source. The bacterial
survival was determined on Petrie dishes (with a full strength culture
medium, by means of seeding on the corresponding cultures).

Simultaneously with the experiments on bacteria was used the
extracellular bacteriophage TCh Vr +, grown on E. coli B B_4 in
full strength and minimal culture media. Adam's method was used to
obtain a bacteriophage with a high titer. The primary lisate
with a concentration of 10^{11} phage particles per milliliter was
centrifuged with subsequent resuspension and culture in nutritive
broth and a buffer to 10^9-10^{10} phage particles per milliliter.

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[4]The research was conducted together with G. A. Leont'yeva and
I. A. Livanova.

The bacteriophage was irradiated together with the bacteria with identical doses in the same glass ampules. The bacteriophage survival was determined by the agar layer method in Rautenschtein's modification with the indicator strain E. coli B. The percentage of survival was calculated according to the ratio of the number of surviving phage particles, subjected to irradiation, to the number of phage particles in the control.

Data on the survival of the bacteriophage TChVr$^+$ in nutritive broth are given in Figure 4. The relative biological effectiveness of the high energy hadrons generated on the target by protons of 70 GeV, calculated with respect to the slope constants of the approximating curves, is between the limits of 1.2 and 4.0 (broth) or 2.5 (buffer), and at individual experimental points was significantly greater [4, 13, 15].

Our attention is drawn to the significant differnces in the evaluation of the relative biological effectiveness obtained according to the approximating curves in the two perfectly identical experiments (Figure 4). Subsequent experiments with a bacterio- phage irradiated in a broth and buffer (ten experiments, having been carried out, showed similar results.

Further, attention is also drawn to the experimental point /13 of the first experiment on Figure 4 for the dosage of 80 krad. The effect calculated according to all remaining data should correspond to a 7.5% bacteriophage survival, while in actuality the survival was equal to 0.01% (a difference of 750 times). This is statis- /14 tically reliable since the standard error of the experiment did not exceed 20%. In our experiment we never found such significant deviation in the case of Cs^{137} gamma irradiation.

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TABLE 2

RELATIVE BIOLOGICAL EFFECTIVENESS OF SECONDARY EMISSION FROM PROTONS WITH AN ENERGY OF 70 GeV ACCORDING TO THE INFLUENCE ON (faba5)

Criterion	Average RBE Values	Calculated Maximum RBE Values
Number of chromosome fragments per 1 aberrant cell-		
first fixation	2.20(a)	3.20
third fixation	2.00(a)	4.50
Number of chromosome bridges per one aberrant cell-		
first fixation	2.11(a)	3.24
third fixation	1.94(a)	3.60
Number of aberrant cells with chromosome fragments-		
first fixation	1.85(b)	-
third fixation	1.52(c)	-
Number of aberrant cells with bridges -		
first fixation	1.67(b)	-
third fixation	1.62(d)	4.70
Number of aberrant cells with bridges and fragments-		
first fixation	1.68(b)	4.88
third fixation	1.52(c)	
Survival of primary root	1.85(c)	
Length of root of 12-day plant	1.64(b)	4.61
Length of root of 9-day plant	1.66(c)	-
Dry weight of 12-day plant	1.60(b)	2.03

[5] The RBE's were calculated: a--by averaging the RBE values for each dose; b--with respect to the angles of inclination of the dosage curve; c--according to 50% effect doses; d--according to a 25% effect dose. Maximum RBE--theoretical maximum value of RBE, determined with respect to the linear component of the dosage curve equations according to ICRP recommendations.

TABLE 2 (cont.)

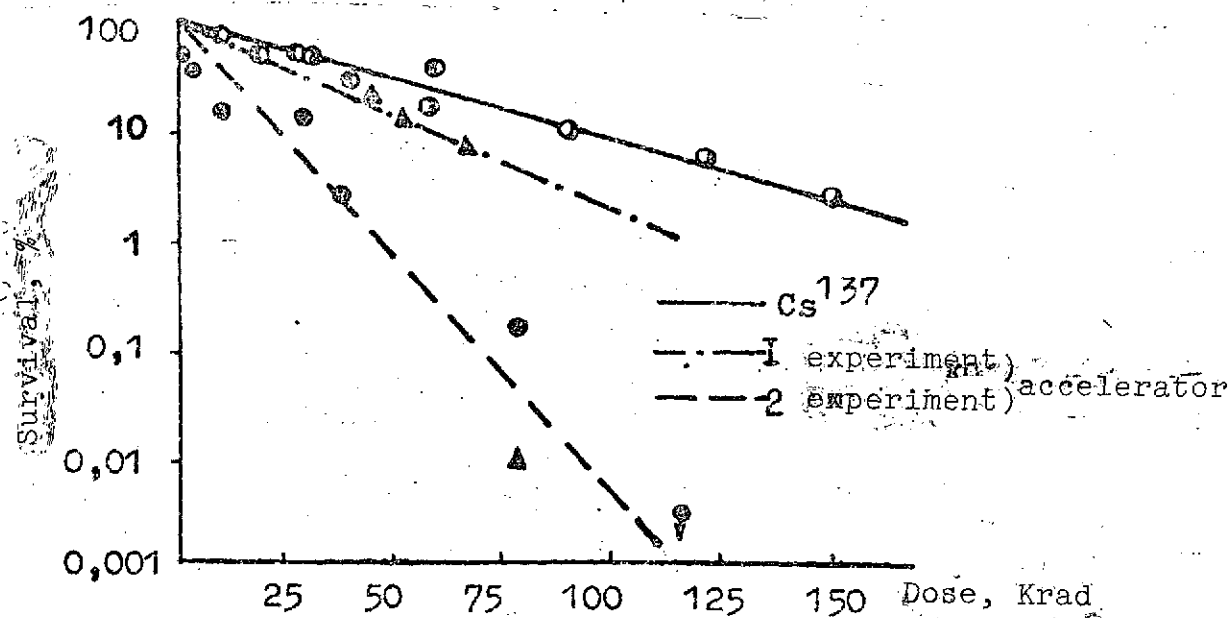|		
Weight of decrease in number of aberrant cells with chromosome fragments	1.74(b)	–
Rate of decrease in number of aberrant cells with chromosome bridges and fragments	1.71(b)	–
Rate of decrease in number of chromosome fragments per aberrant cell	1.54(b)	–
Rate of restoration of growth of primary root	1.85(b)	–

Figure 4. Survival of TCnVr$^+$ bacteriophage in culture broth.

However, in the experimental groups individual scatterings were noted also in the second experiment with the irradiation of the bacteriophage in broth with a dose of 120 krab. The actual survival was less than $2 \cdot 10^{-8}$%, that is five orders of magnitude below that which was expected in correspondence with the approximating curve (10^{-3}%). In the experiment in which the bacteriophage was irradiated in the buffer, individual deviations in survival reached seven orders of magnitude (a doze of 40 krab) and four orders of magnitude (a dose of 80 krab). Subsequent experiments with bacteriophage accelerator irradiation confirmed the possibility of such significant deviations from the approximating curve even including in the cases where the average RBE was around 1.0.

It seems to us to be deserving of attention the fact that all cases of significant deviation in survival were only on the side of its limitation, that is on the side of a sharp increase in the effectiveness of adron radiation.

The RBE accelerator radiation with respect to the survival of E. coli B according to the approximating curves equalled from 0.8 to 3.7 in different experiments. Here also there were deviations on the side of higher effectiveness.

Two experiments with E. coli K-12 (λ) were conducted for the purpose of verifying the possible dosage dependence in OBE coefficients. It was not possible in either experiment to plot a correct approximating curve without an inverted arm (Figure 5).

As a consequence of this RBE values significantly increased with decreasing radiation dosage: in the first experiment from 1.7 to 6.2 and in the second experiment from 0.8 to 3.6.

A more detailed analysis of the materials on the survival of the bacteriophage and E. coli of strains B and K-12 (λ) showed that the experimental point of the majority of experiments may also

be approximated by curves with an inverted arm. The RBE of the accelerator radiation increased with decreasing dosage. Consequently, an increase in the RBE of the accelerator radiation with a decrease in the dosage is characteristic both for the physiological indices of the plant (dry weight and length of the primary route) and a number of genetic injuries (number of cells with fragments or bridges or the number of the latter per cell), and for the survival of bacteria and bacteria phages.
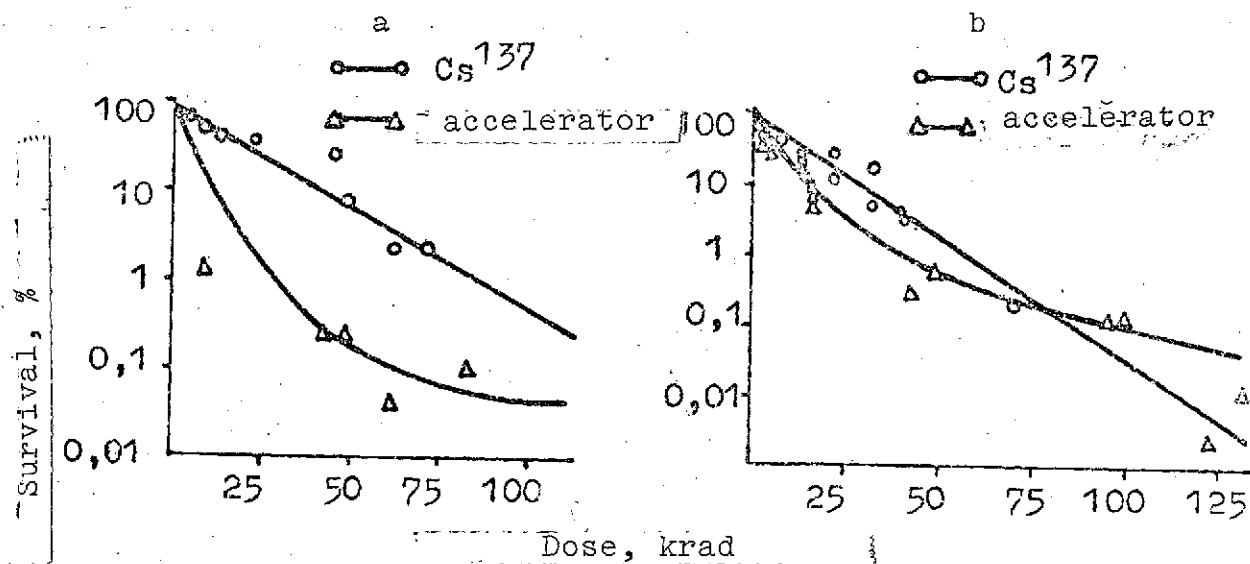
Figure 5. Survival of E. coli K-12 (λ) in minimal medium without glucose; a--first experiment; b--second experiment

MUTAGENIC EFFECTS[6]

In studying the mutagenesis of the bacteriophage TCμVr+ the r-mutance of the TCμV were isolated and identified according to the group rI, rII, rIII. Here the groups are morphologically differentiated according to the ability to form negative colonies

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[6]Research conducted with G. A. Leont'yeva and I. A. Livanova.

on strains of E. coli (B;S;K). All the selected and purified rII-mutants were then investigated for the ability to revert to the pseudo wild type rII⁺. The presence or absence of induced revertants were determined by the "spot" test method. According to this test the rII-mutant was seeded in a titer 2·10⁷ phage particles on a cooled Petrie dish together with a mixture of E. coli K-12 (λ); K₁ in a titer of 2·10⁸ bacteria and E coli B in a titer of 2·10⁷. The addition of the B strain that gives the bacteriophage the possibility of multiplying and undergoing further reversion. When the B bacteria are lysed, then only the revertants rII⁺ continue to multiply on the K strain and thus appear on this background. After solidification of the soft 0.4% agar with the bacteria of the strains K and B and the rII-bacteriophage a drop of chemical mutagen was added to each Petrie dish. The Petrie dishes were then placed in a refrigerator (4°C) for two hours for uniform diffusion of the mutogen. After this dishes were incubated at 37°C for 16-17 hours and then studied for the presence of revertants in the region of the mutogen spot.

We used the following mutogens having a known molecular mechanism of action: nitrous acid (0.2M) hydroxylamine (0.1M), nitrosoguanidine (10⁻³M), change of pH to 3.0, ethylmethanesulfonate (0.02M), proflavin (10⁻³M). Nitrous acid primarily causes transitions, the hydroxylamine more induces transitions and transversions, while changing the pH to 3.0, ethylmethanesulfonate and nitrosoguanidine may promote mutagenesis of the type of transitions, transversions and different deletions, while proflavin acts according to the type of "sign" mutuations, causing insertion or deletion of bases.

The data on the frequency of appearance of the r-mutants of the bacteriophage were approximated by generalizing curves [6, 7, 8]. The identical frequency of mutuations in the case of

the influence of accelerator radiation on the bacteriophage in the broth and in the buffer occurred with doses 2-13 times less than those in the case of the controlled gamma irradiation. In a given dosage range the value of the relative genetic effectiveness (RGE) increased with a decrease in dosage. In addition, the maximum values of the RGE of the accelerator radiation exceeded its RBE with respect to the survival rate. The spectral distribution of r-mutants proved not to be identical for the group rI, rII and rIII. Irradiation of the bacteriophage in a buffer on the accelerator induced 15 times more rI-mutants than on the gamma source.

The results of an investigation of the versions of the rII-mutants are given in Table 3. Nitrous acid induced an identical percentage of reversions of rII-mutants, obtained after a radiation of the bacteriophage in broth both on the accelerator and in the control.

TABLE 3

REVERSION OF rII MUTANTS OF THE BACTERIAL PHAGE TChV
TO THE WILD TYPE (rII BECOMES rII+) UNDER THE INFLUENCE
OF DIFFERENT CHEMICAL MUTAGENS

Media for irradiation of bacteriophage	Chemicals Mutagens	% of inducations of reversions to rII+ from rII-mutants, obtained under the influence of:	
		Accelerator radiation	gamma rays
Culture broth	Nitrous acid	14	14
	Hydroxylamine	21	57
	Nitrosoguanidine	7	28
	pH 3.0	6	43
	Ethylmethanesulfanate	0	14
	Proflavin	0	9
Buffer	Nitrous acid	0	25
	Hydroxylamine	0	89
	Nitrosoguanidine	0	32
	pH 3.0	0	35
	Proflavin	0	18

The hydroxylamine, nitrosoguanidine and changing the pH to 3.0
caused, respectively, 2.7, 4.0 and 7.1 times less reversions in the
rII-mutants, obtained under the influence of accelerator radiation,
than in the case of gamma irradiation. Treatment of the rII-mutants
with ethylmethanesulfonate and proflavin caused no induction of
reversions, while after the control gamma irradiation reversions
were observed in 14 and 9% of the cases, respectively.

A similar analysis, conducted with the rII-mutants, obtained
by irradiation in a buffer, showed that the rII-mutants, formed
under the influence of accelerator radiation, did not at all re-
vert to the rII$^+$ type under the influence of the above mentioned
chemical mutants. At the same time of the control rII-mutants
(gamma radiation) the percentage of reversion attained great
values (from 18 to 89%).

Thus the investigations conducted showed that the biological
effect of secondary emission from 70 GeV protons is characterized
by: (1) exceeding mutagen effectiveness in comparison with lethal
effect, (2) a distinct spectrum of rII-mutations, (3) DNA damage,
inhibiting reversion of rII-mutants under the influence of chemical
mutagens.

All this forces us to assume a different mechanism of molecular
damage under the influence of accelerator emissions and gamma
radiation.

The chemical mutagens we used possessed different molecular
mechanisms of action. This allowed us to more precisely
determine possible changes in DNA. The ethylmethanesulfonate and
proflavin in the case of rII mutants, obtained by irradiation
of the bacteriophage on the accelerator, did not cause reversions
as opposed to the same mutants after the control gamma radiation.
The proflavin is embedded between the bases, causing "fine"
mutations of the "shift in readings frame" type. Large-scale
rearrangements (deletions, inversions and translocations), evidently,

are able to block the appearance of proflavin mutations, and extended deletions--the appearance of ethylmethanesulfonate mutations.

Nitrous acid, hydroxylamine nitrosoguanidine and changing the pH to 3.0 caused significantly less reversions than in the control (irradiation in broth). Consequently, such molecular changes in DNA, as deamination, depyrimidinization, and depurinization in comparison with the control appeared to a significantly lesser degree or did not appear at all under the influence of the above mentioned mutagen in the case of the rII mutants, obtained by accelerator irradiation. This also speaks in favor of the appearance of large scale rearrangements of DNA.

It is interesting that the rII-mutants, which arose under the influence of accelerator radiation in a buffer, did not at all revert with the use of any of the above mentioned mutagens. At the same time the probability of reversions under the influence of mutagens, basically causing transitions, transversions and deletions in the case of rII-mutants, induced by the control gamma irradiation, was close to the data given in the literature. Evidently, it is impossible to explain these results other than by assuming that the accelerator radiation caused unusual damage to the DNA molecule, which is not observed in the case of the action of lower energy radiation and which may block the induction or reversions under the influence of chemical mutagens. Let us recall that the basis of the accelerator emission under investigation consisted of high energy hadrons. The differences in the biological effect of accelerator radiation which appeared, probably, may be connected with the biophysical properties of the strong interactions characteristic of high energy hadrons. Numerous appearances of changes in the DNA due to "burning through" of the coiled DNA chain in the head of the phage by a narrow beam of secondary particles, evidently, may be considered to be characteristic of hadron

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mutagenesis of bacteriophage. Each of the sections may exceed two to three nucleotides, that is, be a different sized deletion (from small to extensive).

All that which has been presented above allows us to assume that the result of the action of high and super high energy hadrons on the DNA macromolecule may be:

a) on the atomic scale--the destruction of any atomic nucleus of the elements comprising the DNA molecule;

b) on the molecular scale--a break in the molecule at any one of its atoms, including at points with the most solid chemical bonds;

c) on the chromosomal scale--more multiple damage with a higher probability of the formation of several chromosome fragments in one cell.

The experiments conducted to study chromosomal aberrations in V. faba after the action of accelerator radiation actually showed that this radiation was most effective with respect to the number of fragments occurring per aberrant cell.

It is known that there is a low revertability of spontaneous rII mutations under the influence of chemical mutagens. In the light of the data we obtained it is possible to assume [Fries, 1964; Critch, 1966, Benzer, 1962], that, evidently, molecular damage not only at the points of location of the least weak chemical bond also plays a significant role in the mechanism of spontaneous DNA damage, and that this may be connected with the fact that it is always possible for radioactive carbon to substitute for any carbon atom of the DNA. The genetic effectiveness of included radioactive carbon is very high [Golenetskiy, 1971; Pluchennik, 1968]. As is well known, cosmic radiation is a constant source of generation of radioactive carbon in the earth's atmosphere.

The overall effect in our experiment was connected not only with the characteristic hadron mechanism, but with the "usual,"

mechanism, characteristic of all types of ionizing radiation.
The influence of the adron mechanism here even in identical
experimental conditions was of a statistical nature. In the case
of its low probability the biological effect of hadrons could be
masked by damage from the "usual" mechanism of action. This,
evidently, is the cause of the significant variability of the values
obtained for the RBE and RGE of secondary emission from 70 GeV
protons.

ANALYSIS OF RESULTS OF BIOLOGICAL STUDIES
IN SPACE

In cosmic radiation the hard component is represented by high
and super-high hadrons capable of strong interaction. Despite the
extremely insignificant portion of the total flux of cosmic radia-
tion for such a super hard component, evidently, it is possible
to expect high biological effectiveness as a consequence of those
properties of strong interaction which are characteristic of high
and super-high energy hadrons. In the conditions of a spacecraft
protection from them by screening or force fields, evidently, is
hardly realistic.

Therefore it is interesting to analyze the results of biological
studies in space and to compare this analysis with the results of
our investigations on the biological effect of high energy hadrons.
For this analaysis we used published materials [Gazenko, Antipov,
Parfenov, 1971; Grigor'yev, Kovalev, 1972; Vaulina et al, 1971;
Delone, Morozova, Antipov, 1971; Dubinin, Kanavets, 1962; Glem-
botskiy et al, 1961; Galkina, Aleksandrova, 1971; Garina, Romanova,
1970; Tsarapkina, Alekseenko, Tsarapkina, 1971; Gaydamakin et al,
1971; Nuzhdin et al, 1965, 1967, 1970 and other studies], and
also materials of the experiment of USA scientists on the Bios-II
satellite and data from the bioblock experiments conducted on
board "Apollo 16 and 17." Considering the great methodological
difficulties for the space experiment in observing all the necessary

experimental conditions, particular attention was turned to experiments with dry aerial seeds as objects the least subject to random fluctuation of experimental conditions.

On the basis of all the data available in the literature it seems to us to be possible to isolate the following features of the results of biological investigations in outer space [2, 14]:

1. The absence of a clear dependence in the expression of the observed somatic and genetic effects (in those cases where they were observed) on the measured radiation dose, duration of the influence of weightlessness and other factors of space flight.

2. The recorded radiation doses, as a rule, are very low. They are often one to three orders of magnitude and more less than the doses which are necessary to produce similar effect in "ground" conditions. This was observed, for example, in N. I. Nuzhdin's experiment on the production of aberrant cells in barley. The attempt to explain these differences by the joint effect of radiation and weightlessness, as the experiment on the Bios-II satellite with an "ordinary" irradiator on board showed, did not prove convincing.

3. Insufficient repetition of results from one experiment to another in the same or close space flight conditions.

4. Different degrees of expression of biological effect in one experiment, when several identical biological objects are exposed at the same time. For example, on the automatic station "Zond-6", which flew around the moon, in approximately one-third of the barley seed samples a significant increase in the production of aberrant cells was observed [Nuzhdin, 1967]. In the remaining samples this was not observed, corresponding to an extremely low value of the measured radiation dose, or it was statistically unreliable. In the experiment of Semenenko and Vladimirov [1962] of five test tubes with Chlorella there was a decrease in the survival rate of only one, however it was very significant.

5. Disagreement in the degree of expression of observed damage, caused by the influence of space flight factors, with ideas of the radiation resistance of biological objects in relation to ordinary ionizing radiation. Thus, space flight factors produced the /19 same yield of aberrant cells both in the case of radiation sensitive, and in the case of radiation resistant source of feeds.

6. The possibility of weakening the degree of expression of the influence of space flight factors by means of chemical prophylaxis. It has been established, for example, that the production of aberrant cells, induced by space flight factors, was significantly lowered with the use of cysteine.

The above mentioned characteristics of biological studies in space forced us to seek an explanation in the influence of a factor which: a) is not considered or is statistically unreliably recorded, b) is biologically very effective and c) not uniformly present at every point in the volume occupied by the biological objects. This factor, evidently, may be the superhard component of cosmic radiation with an energy exceeding dozens of giga-electron volts. Its origin is connected with nonstationary sources, which forces us to assume that significant fluctuations in spectrum and flux are characteristic of it. It may be expected that as a result of the interaction of primary galactic protons and other super high energy adrons with the body of a spacecraft a narrow beam of secondary emission, which will contain multiply charged nucleii, adrons of different types and charges, and "ordinary" radiation, will act upon the crew and biological objects. This will create extremely irregular energy absorption in microgeometrical volume, which are several orders of magnitude less than the volumes of the ionization chambers and activation detectors used. For this reason the latter measured only an average dose, and not the dose actually absorbed by individual macrogeometrical volumes.

Thus, in model experiments with hadrons on an accelerator and in space experiments there were revealed such general characteristics of the biological effect of the factors studied as the possibility of high biological effectiveness with significant variability in its degree of expression. In both cases there is noted as a characteristic feature a certain multiplicity of structural damages (chromosome fragments) and a certain specificity of changes (poor revertability of mutations, high probability of the appearance of deletions of extended nature). At the same time there is shown the influence of reparation processes on the degree of expression of the induced chromosomal aberrations and the possibility of decreasing them by chemical prophylaxis.

All the observations discussed above have a good explanation if we consider that in addition to "ordinary" radiation, having a comparatively low RBE and RGE, in both cases (on the accelerator and in space) high and super-high energy hadrons acted with their characteristic statistical regularities of interaction with matter, and the characteristic specific hadron biophysical mechanism, determining their possible high biological effectiveness.

Posing the problem in this way forces us to specify a number of new requirements both with respect to dosimetry (microdosimetry, linear energy transformation measuring), and with respect to biological objects, in particular, so as to be able to separate general effect on an entire biological object from local effect connected with the statistically comparatively rare event of local specifically hadron damage.

DISCUSSION

The study of the biological effectiveness of strong interactions of high and super-high energy hadrons was begun with experiments with the hybrid secondary flux generated in the region of the primary target of a 70 giga-electron volt proton accelerator. The

multicomponent composition and broad energy spectrum of the secondary
emission complicated the study of the primary factors determining
biological effectiveness. However, it was necessary to consider
those real conditions for which it was necessary to evaluate possible
biological danger and to obtain data both for the radiation-hygienic
normalization of work on the accelerator and in other institutions
and establishments using high and super high energy radiation,
and for the purposes of space biology. The "hottest" zone on
an accelerator is the region of the primary targets, and the most
significant force here and in a spacecraft is precisely the hybrid
flux of secondary emission formed by a primary particle of super
high energy.

The investigations conducted showed that the biological effect-
iveness of the secondary emission from 70 giga-electron volt protons
in comparison with the control Cs^{137} gamma radiation may be higher.
It may be higher than was expected on the basis of the traditional
concepts, utilized in radiation-hygienic normalization, of a
unique connection between the biological effectiveness of radiation
and the average values of linear energy transmissions. We showed
this with respect to a whole number of factors: the survival rate
of bacteria and phages, the survival rate of V. faba shoots, the
decrease in their weight and the length of the primary root,
chromosome damage in V. faba (both with respect to the number of
cells with chromosome aberrations and with respect to the number
of aberrations per cell), the frequency of bacteriophage muta-
tions, and also with respect of several specific indications of
mutagenesis.

In order to explain the results we obtained it was necessary
to evaluate the possible influence of the following conditions
of conducting the experiment: the magnetic field intensity in
the region where the biological objects were placed and differences
in the power of the irradiation dose of the control and test groups.

The available literature does not give an unambiguous response
to the question of the possibility of magnetic field influence on
biological objects [Barnoti, Lanch, Tobias, 1973]. If it is ack-
nowledged that the magnetic field can influence the effectiveness
of action of radiation, then this occurs only in the case of com-
bination with small radiation doses, for example less than 8 krab
for plant seed and insect larvae. The maximum decrease in survival
rate with small doses in these conditions was less than 40%. Measure-
ment of the magnetic field intensity at the point where our biological
objects were located on the accelerator [Komarov et al, 1969] showed
that most of these places were not at all subject to the influence
of any significant magnetic field. The only exception is the
region at a distance of 15-16 meters from the target where a
sharp peak in the magnetic field intensity, reaching 1.0-1.8 Ke,
was noted. Comparison of the dosage curves of the survival rate of
bacteriophage and bacteria, and also of various effects on plants
[3, 12, 14] did not reveal any changes in the effectiveness of
irradiation for the above-mentioned regions with a magnetic field
intensity peak. This gave us the basis for excluding magnetic
field influence in an explanation of the effectiveness of the
radiation studied which we observed.

Verification of the influence of differences in dosage power
was made in special experiments with gamma irradiation of E coli
K-12 (λ) in an M-9 medium (without glucose) and the TChVr bacterio-
phage in culture broth at 3; 47; 486 and 3617 rad/min. Variation in
dosage power did not prove to have any influence on the bacterio-
phage survival rate. At the same time it was shown that the
dosage power clearly influences the survival rate of the intestinal
bacillus. In addition it was shown that this was different for
different levels (doses of 10, 20, and 40 krad were tested):
minimum for a dose of 40 krad and maximum for 10 krad. The survival
rate increased in regular fashion upon transition to dosage powers

of less than 486 rad/min. The fact that with a dosage power of 47 rad/min the effectiveness of irradiation was lower than with 486 rad/min was important for us. In spite of this the effectiveness of accelerator irradiation, although it was with less dosage power (20-30 rad/min), proved to be significantly higher than the control irradiation (475 rad/min). If appropriate correction is made then the RBE of the accelerator irradiation becomes even higher (by approximately 1.2-3 times).

The high effectiveness of protons and secondary emission with energies exceeding 1-10 GeV was unexpected from the point of view of the accepted concepts of the existence of a specific connection between the mean values of linear energy transmission and the RBE, since they are characterized by low mean values of linear energy transmissions, equal to approximately 0.2-0.3 KeV/μm, according to the data of Smith [1967] and Baarli [1971]. Actually, as is seen from the data given on Figure 6, the biological effectiveness of nuclear particles drops in proportion to the decrease in the mean values of the linear energy transmission below 100-40 KeV/μm, which is observed, in particular, even with an increase in proton energy from several KeV to hundreds of MeV. The RBE value here becomes less than 1.0; it was assumed that this regularity will hold even in the case of a further increase in the energy of protons and the secondary emission formed by them [Cowen, 1967]. Shortly thereafter, Smith [1967] showed that the RBE of μ-mesons with an energy of 8 GeV as was predicted, is equal to 0.7 with respect to the ability to cause chlorophyll mutations with the irradiation of maize seeds.

Moreover, already from theoretical calculations using the Monte Carlo method [Neufeld, 1966, 1969; Alsmiller et al, 1970] even with the use of the generally accepted dependence of the quality factor QF on the LET it followed that the quality factor of hadron radiation, and consequently also the RDE must continuously increase

beginning with 40-60 MeV for charged hadrons (excluding -π-mesons in the Bragg peak) and with an energy of 400 MeV for neutrons [15].

From this pointof view the results we obtained are not unexpected. Moreover, they are confirmed in the works of other authors. Ryzhov et al [1967] obtained an increase in RBE from 1.0 to 1.15-1.20 by raising the proton energy from 126 to 510 MeV (experiments on dogs). On plant objects the RBE of 650 MeV protons is approximately 2.0 [Nevzgodina, Pol'yen, Gertsusskiy et al, 1967, 1970]. The OBE of 400 MeV neutrons rises to 1.5-5.9 with respect to the influence on the turbidity of the crystalline lens, weight of the testes and survival rate of the spermatogonia of mice.[Baarli et al, 1971]. The RBE of protons of 2.3 GeV and 28 GeV and π-mesons of 8 GeV is 1.3-5.2 with respect to the effect on the crystalline lens of the eye, weight of the thymus, spleen and gonads of mice and with respect to the induction of chlorophyll mutations in maize [Smith et al, 1967; Monto et al, 1969; Lezho et al, 1971].

All the above signifies that there are serious difficulties /22 of a fundamental order in predicting the biological danger of superhard radiation. The concept of mean linear energy transmission does not make it possible to make experimental and theoretically well founded predictions. In equal values of mean linear energy transmissions the biologically effectiveness may differ by many times. Thus, π-mesons as opposed to μ-mesons of the same energy (for example, 7-8 GeV) have identical mean values of linear energy transmissions (in the given case equal to 0.25 KeV/μm) and at the same time with respect to their biological effectiveness differ by seven times [data from Smith et al, 1967]. We see the cause of this in the fact that a π-meson is a hadron and a μ-meson is a lepton, not capable of strong interactions in the given condition.
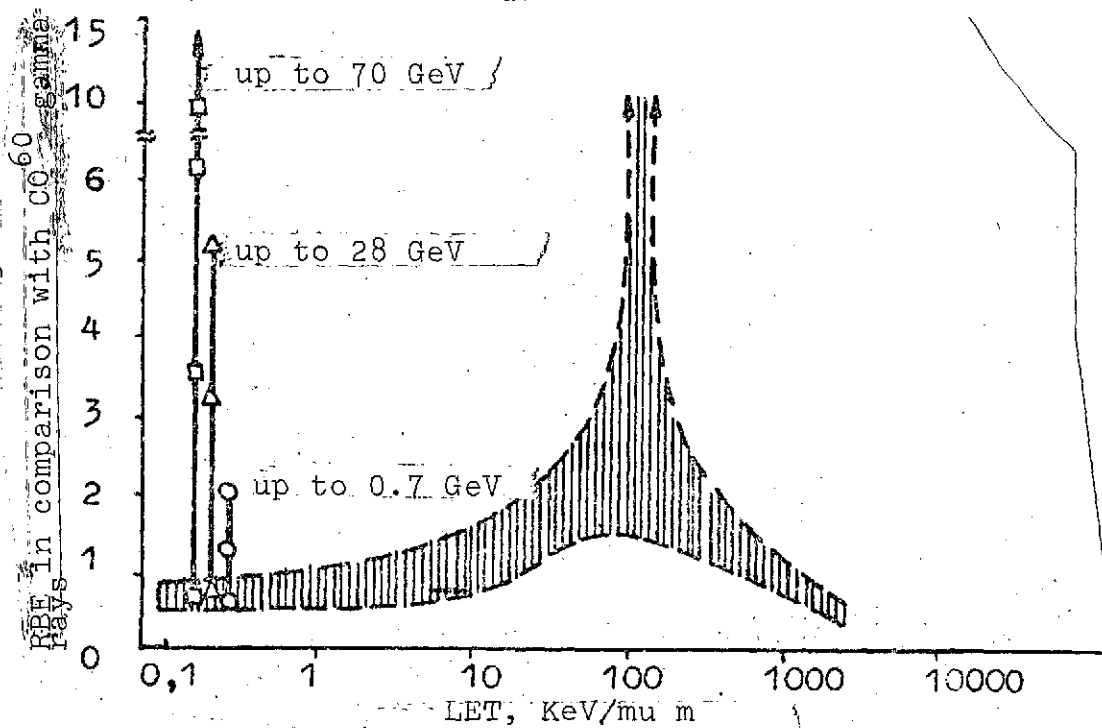
Figure 6.   Relationship of relative biological effectiveness and mean linear energy transmissions.

From this point of view there is great interest in Baarli's data that 400 MeV neutrons proved to be more effective with respect to an absorbent intended to attenuate neutron energy for the purpose of obtaining linear energy transmission in the area of the Bragg peak due to the formation of nuclear splittings of the "star" type. Consequently, even in this case the greatest effect could be hypothetically connected with the effect of high energy hadrons with their characteristic narrow beam of secondary particles.   The neutrons attenuated by the absorbent were no longer capable of generating such narrow beams of secondary particles.

Our experiments showed that the biological effectiveness of high energy hadrons may significantly, by two to five times and more, be raised with a decrease in the radiation dose. This clearly follows from such indicators as the frequency of chromosome damage in V. faba and the survival rate of E coli K-12 (λ). On curves of the bacteria survival rate in such cases there appears an inverted branch which is often explained by the heterogenity of the cell population or by the appearance of endogenic protective substances. However, in the case of the control gamma irradiation in these same conditions the curve has a normal appearance. Moreover, it is necessary to consider that in our experiment the control and test samples were prepared simultaneously and from the same cultures. It is very characteristic that a similar dosage dependence of the RBE of hadrons can also be discovered by analyzing the survival rate of the phage--the object the least dependent on the random fluctuations of experimental conditions (Figure 7). A comparison of equally effective doses shows an increase in RBE to 10 and more with a decrease in the radiation dose. A similar dependence is obtained by Baarli et al [1971] with respect to the influence of 400 MeV neutrons on the survival rate of spermatogonia and Sullivan et al [1970] for negative pions.

The next feature of our experiment is a certain variability of the biological effectiveness of accelerator radiation from experiment to experiment and within the limits of a single experiment. The existence of such a spread of data was also noted by many investigators in space experiments, which has already been mentioned. It is important that they are always observed in the direction of more effectiveness. In our experiments the difference are such as if the radiation doses of individual experimental groups unexpectedly fluctuated by 2 to 5 times and more (Fig. 7). The given effects here proved to be unnoticed by the tracking activation detectors we used and the ionization chamber located at the end of the radiation beam under investigation. After careful

analysis failure to observe the conditions necessary for performing experiments identically was excluded. Moreover, such fluctuations were not observed in the control group.

Among other results, which we obtained, the following have primary significance:

1. The relative biological effectiveness of accelerator radiation with respect to somatic and cytogenetic (number of aberrant cells) test was close to the RBE of this radiation with respect to the influence on the rate of post radiation recovery, evaluated according to the number of aberrant cells according to change in the weight of shoots. Consequently, it may be assumed that even in the case of the influence of radiation under consideration recovery processes play a significant role in determining the observed damage to metabolizing objects.

2. The RBE of the radiation studied was greatest with respect to the effect on phages--non-metabolizing objects, not having damage-repairing systems, which confirms the first proposition.

3. The post radiation recovery speed in the given dosage range increased with increasing irradiation dosage both for the experimental and for the control groups. Then it began to decrease.
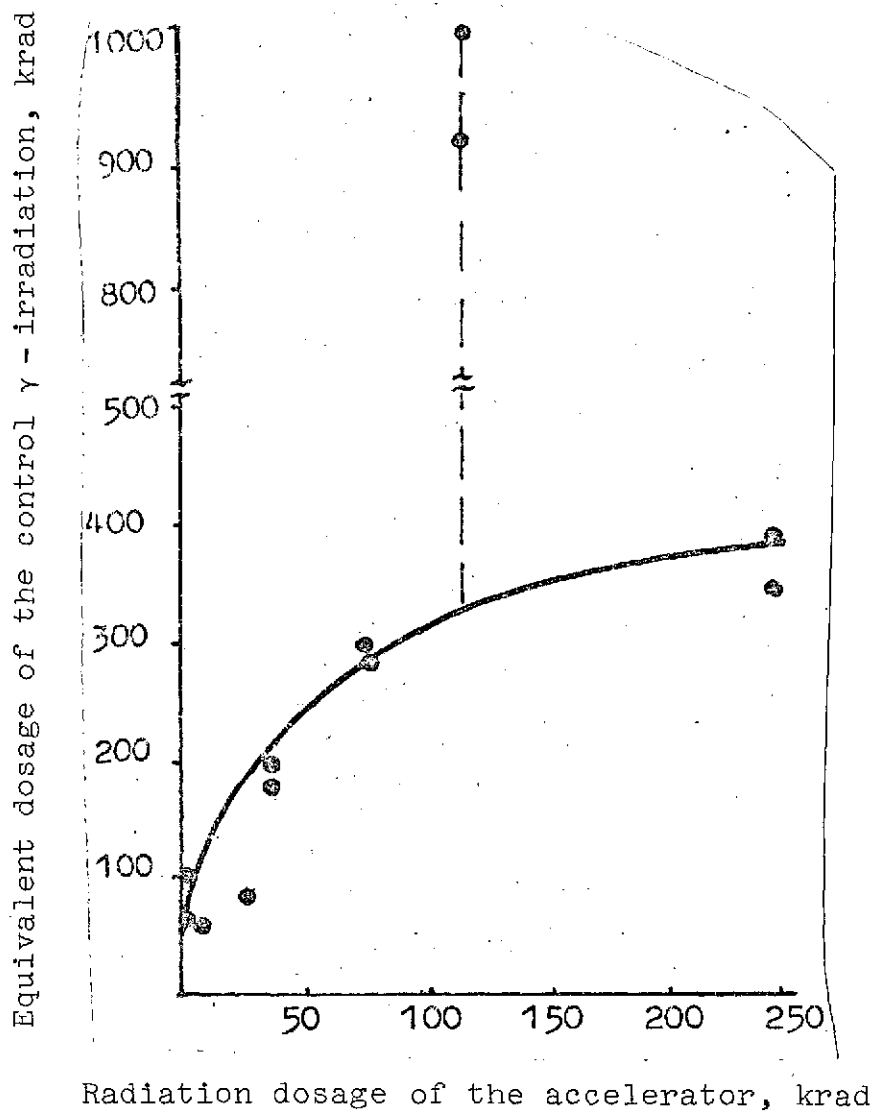
Figure 7. Correlation of equivalent doses of acceleator radiation and control γ-irradiation for a bacteriophage in a culture broth.

The general biological law of approximate proportionality of the recovery speed in the given dosage range of intensity of damage to man and mammals, which we obtained previously, held true both for the growth of plant seeds, and for chromosome damage.

4. On plant objects the mean RBE values of the radiation studied decreased with respect to chromosome aberrations with the transition from the first to the third fixation, that is with increasing time of the effect of reparation processes. This may be explained by the fact that the accelerator radiation, causing a greater degree of chromosome damage than in the control, was not able to produce an adequate degree of activation of reparation processes, evidently, due to the more significant difficulties in the functioning of these processes than in the control.

5. Of the physiological and cytogenetic factors in plants, accelerator radiation had the least RBE value with respect to the rate of decrease in the number of chromosome fragments per aberrant cell. Probably the greatest difficulties in repairing damage caused by accelerator radiation occurred in the processes pre- /24 ceeding and determining chromosome fragmentation.

6. Of the physiological and cytogenetic factors in plants, accelerator radiation had the greatest RBE value with respect to the number of chromosome fragments per aberrant cell. This indi- cates the very high probability of simultaneous damage to several chromosomes in one cell.

7. According to a number of indicators (chromosome damage, root length and dry weight of Vicia faba; survival rate of E. coli K-12 (λ) and the TChVr+ bacteriophage the RBE of accelerator radiation increased by two to five times and more with a decrease in the dose of irradiation. This type of relationship, the literary data and calculation of the maximum RBE, according

to recommendations of the ICRP, indicate that the RBE of the radiation studied, particularly with respect to influence on genetic structures, may be significantly higher in an unstudied small dosage range than was obtained in the present study in the case of higher doses. The results of biological studies in space also speak well for this hypothesis.

8. The spectrum of bacterial phage mutations, caused by accelerator radiation, differed from the spectrum of mutations caused by gamma irradiation. These differences are most significant with respect to the number of rI and rII mutations of the bacteriophage irradiated in a buffer. This led to the assumption of specific characteristics in the molecular mechanism of the genetic effect of accelerator radiation.

9. The rII-bacteriophage mutations caused by the radiation studied, as opposed to the rII-mutations, arising under the influence of gamma radiation, proved to be incapable or little capable of reverse mutations (reversion to the wild type) with the use of chemical mutagens with a known mechanism of action. Consequently, the molecular nature of the damage caused by both types of radiation is not identical.

10. Cases of an unexpectedly significant increase in the RBE, at individual experimental points exceeding the mean values of the RBE, determined by approximation of all experimental data, were noted in the case of the influence of secondary emission. This indicates a varying factor in the effect of the radiation studied, the biological effectiveness of which may be very high. Analogous data are also obtained in space studies.

It is impossible to explain the discovered characteristics of the biological effect of accelerator radiation with the traditional radiobiological concepts valid for analyzing the results of the

influence of already studied types of radiation with energy lower than 0.5 giga-eV. It is necessary to consider some of the physical characteristics of the secondary flux generated on a target by protons with an energy of 70 giga-eV. Such an examination showed that this flux is comprised of nucleons and mesons of different types and charges, capable of strong interaction, that is, adrons. Therefore in the present study the biological effectiveness of accelerator radiation is connected with the characteristics of the effect of high energy hadrons. Their mean spectral energy in the experiment was within the range of 10 to 40 giga-eV.

The first characteristic of the effect of high energy hadrons is that the result of each strong interaction may be the multiple generation of secondary particles, also primarily hadrons of still quite high energies. Among them there are also heavy multilply charged fragments and anti-protons. These processes are of a statistical nature. For example, Figure 2 shows a photograph of the statistically very rare result of the strong interaction of one pion with a carbon nucleus in a propane chamber. It is possible to count more than 50 of only the tracks of charged nucleons and mesons. Uncharged particles--neutrons and null-mesons (π-K-and others), comprising a significant part of the flux, are not visible on the figure. Rarely appearing heavy particles may possess high biological effectiveness [Tobias et al., 1972; Brasted, 1962; Todd, 1967; Bond, 1971; Ryzhov et al., 1967, 1970] and introduce a significant contribution to the variability of the biological effect.

The second characteristic of strong interactions of high energy hadrons is the very small angular distribution of the /25 tracks of the nuclear particles formed. This is also quite clearly visible on Figure 2. A narrow beam of secondary particles is formed, continuing, in the direction of flight of the hadron, which

entered into strong interaction. Since the origin of the beam has
atomic dimensions, then in some proximate region the density of
secondary nuclear particle tracks will be extremely high--by several
orders of magnitude higher than in a neighboring region, not gripped
by a narrow beam of secondary hadrons, where only electron-proton
scattered radiation will act. In proportion to the distance from
the point of strong interaction the density of the beam of secondary
adrons decreases, and their energy drops. This leads to an extreme
irregularity in the density of the energy absorbed by a biosubstrate.
Microsections are created having extremely high doses of irradiation.

The third characteristic of the effect of high energy hadrons
is their capacity for nuclear interaction and for splitting the
nucleus of any element of a biosubstrate, since in the case of such
high energies resonance peaks of nuclear interaction are practically
absent. The formation of mesoatoms and mesomolecules, characteristic
for the interaction of low energy pions, with the subsequent formation
of chemically unusual molecules, is not excluded.

The above enumerated characteristics do not exhaust all the
possible characteristics of the strong interaction of high energy
adrons, the physical aspects of which still greatly remain the
subject of future investigations by large scientific teams. However,
that which has been presented shows the entire complexity and
possible specifics of the interaction of high energy hadrons
biological tissues and macromolecules. They may be drawn upon for
interpreting the characteristics of the biological effects of
secondary emission and from 70 giga-eV protons, revealed in the
present study.

The main significance of the results of the present study is
that they show the possibility of high biological effectiveness
of high energy hadrons particularly with respect to influence on

genetic structures, and, in the case of small doses of irradiation, some specifics of the damage to the DNA molecule and the great difficulties of using traditional concepts in evaluating the possible biological danger of this radiation.

In the case of attempts to extrapolate the results obtained from these investigations with respect to man it must be considered that with an increase in body dimensions the probability of the absorption of the energy of a secondary hadron beam will increase, and the effectiveness of the biological effect of each active strong interaction will also increase. According to available literary data even the transition from mice to rats leads to a significant increase in the RBE of strongly interacting radiation [Bond, 1969]. Moreover, it is necessary also to consider the fact that the damage caused by high energy hadrons is repairable to a certain degree, but the speed of recovery processes in man is very low.

The studies conducted showed that the investigations pushed into a new previously unknown region--the biophysics of strong interaction of high and super-high energy hadrons. These are characterized by low mean energy transmissions and a number of biological effects. In view of the great practical and theoretical interest let us examine this area of linear energy transmission, taking account of the available information about the connection between biological effects and mean linear energy transmissions. [10, and also Tobias, Todd, 1964; Berendsen et al., 1971]. We shall arbitrarily divide the range of possible linear energy transmission values into four zones.

1. The zone of low linear energy transmissions, approximately from 0.3 to 10 keV/μm, is the most studied. This is irradiation, x-ray radiation of different energies, electrons, protons with an energy of from 7 mega-eV to several hundred mega-eV, deutrons of

10 mega-eV, fast neutrons with an energy of more than 14 mega-eV. For all metabolizing objects the RBE of this radiation is comparatively low and approximates the effect of hard gamma rays. The RBE slowly rises from values somewhat less than 1.0 to values somewhat exceeding 1.0 in proportion to the increase in linear energy transmission in this range. The damage is repairable and reparation processes are easily performed. The irreversible part of the damage is small. The oxygen effect is well pronounced. Chemical prophylaxis is effective. Damage is easily modified. The influence of dosage power is significant. Evidently, even multiply charged nucleii (He, C, O, Li, B, Ne and others) with energies sufficient for the linear energy transmission to become less than 10 keV/μm may possibly belong in this zone. Thus, for example, for this the energy of helium nucleii must be more than 50 mega-eV.

II. A zone of significantly increased biological effectiveness with an increase in the linear energy transmission value from 10 keV/μm to approximately 50-150 and more rarely 200 keV/μm. At the same time the irreversible portion of the damage significantly increases, the repairability of the damage decreases and the rate of reparation significantly slows down. The oxygen effect, the influence of dosage power, radiation protective measures and modifying factors decrease or are completely absent. These are neutrons with an energy from 10 to 0.2-0.4 mega-eV, protons approximately from 5 to 0.2 mega-eV, helium nucleii from 20 to several mega-eV, nucleii of other elements, accelerated to the appropriate energies. For example, for carbon nucleii this energy is around 100-120 mega-eV. In this zone maximally high RBE values are noted for all complex metabolizing biological objects. However, the influence of such radiation on phages and certain bacteria, on the other hand, decreases with an increase in the linear energy transmission.

III. With a further increase in the linear energy transmission
the biological effectiveness of radiation begins to sharply de-
crease and becomes equal to less than 1.0. In this zone the oxygen
effect is insignificant or completely absent. There are essentially
no data on the extent of the irreversible portion of damage and
the repairability of the latter. It is assumed that damage in this
zone may be only insignificantly modified. This zone includes
thermal neutrons, helium nucleii with an energy less than several
mega electron volts, multiply charged nucleii (for example: see
Ne, O and others) with energies of several dozens of megal electron
volts and fission fragments of uranium and plutonium.

A non-hadron interaction mechanism, connected with the ionization
and excitation of atoms, and more rarely with elastic nuclear
interaction, is common for the radiation of all three zones.

IV. On the basis of an analysis of our investigation and the
information in the literature it appears to be possible to speak of
a new fourth zone with a hadron mechanism of radiation action.
Here there are low mean values of linear energy transmission (less
than 0.3 keV/μm), however, high values of the RBE of radiation are
possible. Here both actively metabolizing complex biological ob-
jects, and also bacteria and bacteriophage, may have a high
RBE. Recovery processes are active, although somewhat hindered.
Chemical prophylaxis is possible. Consequently, there are features
here characteristic both for the first and second zones. However
there are also characteristic features. The most interesting of
them are: the significant variability of biological effectiveness,
the high genetic effectiveness, multiple damage to cell structure,
a distinct spectrum of mutations and a different molelcular
mechanism of damage, in which the firmness of chemical bonds does
not play a decisive role. All types of corpuscular radiation,
which are high energy hadrons belong in this zone.

This fourth zone of radiation is very important for space biology. High and super-high energy hadrons appear to us to be the main and most difficult to overcome obstacle in the business of providing for safety on long space flights beyond the limits of the earth's radiation belt.

CONCLUSION

An analysis of the results of experimental investigations on an accelerator and data in the literature on the biological effect of high energy radiation and the factors of space flight indicated the great theoretical and practical importance of studying the biological effect of high energy hadrons. This direction of research is connected with basically new biophysical processes, with which earlier radiation biology and medicine had essentially nothing to do.

A number of theoretical concepts, well justified in non-hadron radiobiology, proved to be difficult to introduce into this new field of knowledge. Strong interactions of high and super-high energy hadrons are characterized not only by a biologically effective narrow beam of secondary particles, but also by an extremely varied spectrum of them with respect to the types of nuclear particles and with respect to energy. Hadron biology from this point of view is a more general field of knowledge than, for example, the radiobiology of neutrons, protons and so forth. Hadron biology is characterized by the simultaneous manifestations of effects which previously were observed only in the case of the effects of radiation with low linear energy transmission (for example, the active role of recovery processes),or only of heavy nuclear particles (high RBE and RGE) and so forth. Verification of the existing basic theoretical concept in these conditions makes it possible to introduce corrections into many of them, for

the other part to define the limits of applicability and to remove from the the value of general regularity.

At the present time great attention is given to the problems of the biological effect of heavy nuclear particles. This is necessary first of all for space biology. In analyzing the experimental material obtained in space conditions it is necessary to bear in mind that the strong interactions of high and super high energy adrons may be the source of multiply charged nucleii. These processes are probable in the case of a collision of a galactic proton or other particle (hadron) / of super-high energies with the body of a spacecraft. We consider that the most significant influence on a spacecraft crew is not individual galactic multi-charged nucleii, but the entire broad spectrum of secondary particles of hadron interaction, from which multiply charged nucleii may possibly appear.

The effects which at the present time are connected with the action of cosmic heavy particles, in fact, as we assume, may also be produced by the realization of strong interactions of high energy hadrons. We have in mind, first of all, micro-local damage to and fusion of tissues [Tobias, 1972; Bond, 1971; Byuker, 1973]. Here also it is possible clearly to delimit the effects, produced by a heavy particle and by hadron interactions, if we photograph the microlocal track distribution. A linear-extended distribution of ionization along the course of the particle track is characteristic for a high energy heavy particle. In rough approximation this is a line or narrow band. The tracks cannot begin at the center of an object (tissue). It is necessary to trace the point where the particle enters the object. The strong interaction of a high and super high energy hadrons gives rise to a narrow beam of many tracks, which gradually diverge. As a consequence of this, in rough approximation we have a cone, in the expanding portion of which the

track density rapidly drops.

Thus, the proof of the action of a heavy particle of high or super high energies may be a narrow expansive band of microdamage and microfusion of tissue, proceeding from the edge of the tissue or objects. The strong interaction of a hadron of high or super-high energy is characterized by the appearance at a point in the tissue or object of microcenters of damage and fusion, which should be in the form of a trunkated cone with attenuation of damage in the expanding part of the cone. Such damage is not connected with the edge of the tissue or objects.

In both cases there is an extremely concentrated liberation of energy in microgeometrical volume of tissue. For the majority of the cells in these volumes the damage is so intense that they perish. The damage is eliminated with the death of the cells. In radio sensitive tissues this may take place very rapidly (hours, days), considering the microlocal nature of the damage with the preservation of the basic functions of the tissue system. It is another matter in radio-resistant tissues, for example nervous and muscular tissue. In them the processes of the development of damage proceeds slowly [1], and the elimination of damaged and dead cells is slow. This forces us to turn particular attention /28 to the microorganic symptoms of disturbances in the nervous system [Tobias, et al., 1972] and other radio-resistant systems (endocrine, muscular) in analyzing the effect of the factors of space flight.

Unquestionably, hadron biology has taken only its first step. The research will obtain its further development both in the experimental and the theoretical plane. However, our knowledge in this region is such that even today, it seems to us, temporary recommendations of a clinical plan for providing for radiation safety may be proposed.

Temporary Recommendations of a Clinical Plan

1. For radiation-hygienic normalization in conditions of the possible influence of corpuscular radiation of high and super high energies it is necessary to consider:

a) The possibility of the high biological effectiveness of high energy hadrons exceeding the RBE in quality factor resulting from traditional concepts of a rigid connection between the latter and mean linear energy transmissions;

b) The higher effectiveness of high energy hadrons with small doses of radiation and with respect to genetic tests.

2. In the clinical care of persons working in zones with the possible influence of high energy hadrons.

a) It is useful to regularly observe the background of chromosome damage in the leukocytes of the blood with automation of chromosome analysis by contemporary machine methods;

b) It should be borne in mind that the multiplicity of chromosome damage in each cell, for example with respect to the number of chromosome fragments per cell is the most sensitive test;

c) It should be considered that the genetic danger may be above that determined according to chromosome aberrations in blood cells;

d) In the case of discrepancy between dosimetric and biological indicators preference should be given to the latter, since possibly significant increases in the effectiveness of hadron action are reflected only by biological indicators;

e) Particular attention should be given to microorganic symptoms on the part of the central nervous system and other organs in which cellular regeneration of tissues is not expressed (endocrine, muscular, etc.), considering that a comparatively long

period is necessary for its development.

Zone Forming Fungi --A Convenient Object
for Space Investigation

For the further study of the biological effect of high and super-high energy hadrons it is necessary to continue investigation both on the accelerator and in space. It is expedient to conduct these investigations on the accelerator in the field of a hybrid flux of secondary emission from 70 giga-eV protons and on pure bundles of mesons, neutrons and protons of super high energies. Considering that the dosage power of radiation of pure beams is very small, the use of objects sensitive to extremely low doses of radiation deserve particular attention. The experiment by Baarli et al. on using the survival rate of the spermatogonia of B mice deserves fixed attention in this regard.

In the light of the biophysical characteristics of high and super-high energy hadrons there arose a special necessity for biological objects which would make it possible to separate the general effect of radiation on the whole object from the microlocal effect connected with the strong interaction of a hadron or with a multiply charged nuclear particle. In seeking for such an object Ye. Ye. Sel'kov proposed that attention be turned to the so-called zone forming fungi. Specialists in biorhythms are also interested /29 in these objects.

It is known that in the biophysics of complex processes and the general theory of regulation in living systems an important place is occupied by investigation of the nature of biological hours and seeking possibilities of changing the general reactivity and stability of organisms by means of controlling basic biological rhythms. In spite of the fact that fundamental data has been gathered on individual problems (the autoscillatory nature of the operation

of any physical-chemical polyenzymes, systems and regulatory processes, the circadic periodicity of the mitotic and functional activity of tissues and organs and the reactivity of the organism, the influence of the sun on the Earth's biosphere, the high biological effectiveness of heavy cosmic particles and super-high energy hadrons, much of these problems remain unclear and far from practical utilization.

It is assumed that experiments in space with zone-forming fungi will make it possible to move forward in the study:

1. Of the joint influence of all factors of space flight on the physiological mechanisms of basic biological rhythms connected with the growth rate of cells and the periodicity of the change of their forms of activities and multiplication by means of comparison of zone formation on Earth and in space;

2. Of the possible microlocal influence of cosmic multiply charged nucelii and super-high energy hadrons on the processes with respect to sections of asymmetry, arythmia and breaks in zones of spore formations;

3. Of the influence of possible genetic damage by the combinations of all factors of space flight or the local radiation factor on the processes studied by means of reseeding whole and changed sections of spore formation zones of previous fungus cultures with subsequent observation of the development of the fungus and its cultural properties.

Progress in the study of these questions will make it possible also to explain the relationship between internal-cellular factors (periodicity of physical-chemical, polyenzyme and regulatory processes) and external factors for the organism and its system in defining basic biological rhythm (geomagnetic, georadiational and other cirque periodicities).

In subsequent experiments the research may be made more complex by means of studying:

a) the biophysical and biochemical mechanisms of controlling the basic biological cellular rhythms by means of introducing chemical substances, facilitating or hindering the flow of synchronous processes, before the experiments into the culture medium or after the formation of zones in individual portions;

b) the influence of the factors of space flight on the ability of the fungus to resynchronize its light regime and other conditions with continuous periodicity, not coinciding with terrestrial rhythms.

Preliminary work with museum strains of zone forming fungii and random observations have permitted B. M. Kasatkin in our laboratory to isolate the Pushinskiy strain of Actinomyces levoris with particularly clear rings of spore formation on a solid culture medium. His subsequent study, conducted together with A. K. Zarubina (Moscow State University), showed that its basic values are: a contrastive visually observable difference in the ring zones of mycillium (transparent rings) and zones of spore formations (a projecting arch of white color), well visible against a black background (Figure 8); the capacity for self maintenance of synchronization of spore formation up to the formation of seven and more rings; a convenient range of periodicity of spore formation, from 4 to 10 days for each new ring; the possibility of growing a fungus in hermetically sealed Petrie dishes due to its comparatively low air requirement; the possibility of selecting dishes for experimentation after verification of the degree of standardization of fungus growth with respect to the first ring of spore formation; the preservation of the spore formation rings formed for a month and more.

At the present time the biology of the fungi has still been insufficiently studied. The appropriate investigations are being

conducted and the Institute of Biological Physics, Academy of
Sciences, USSR (A. Kh. Akhmadieva, A. P. Savel'yev, A. B.
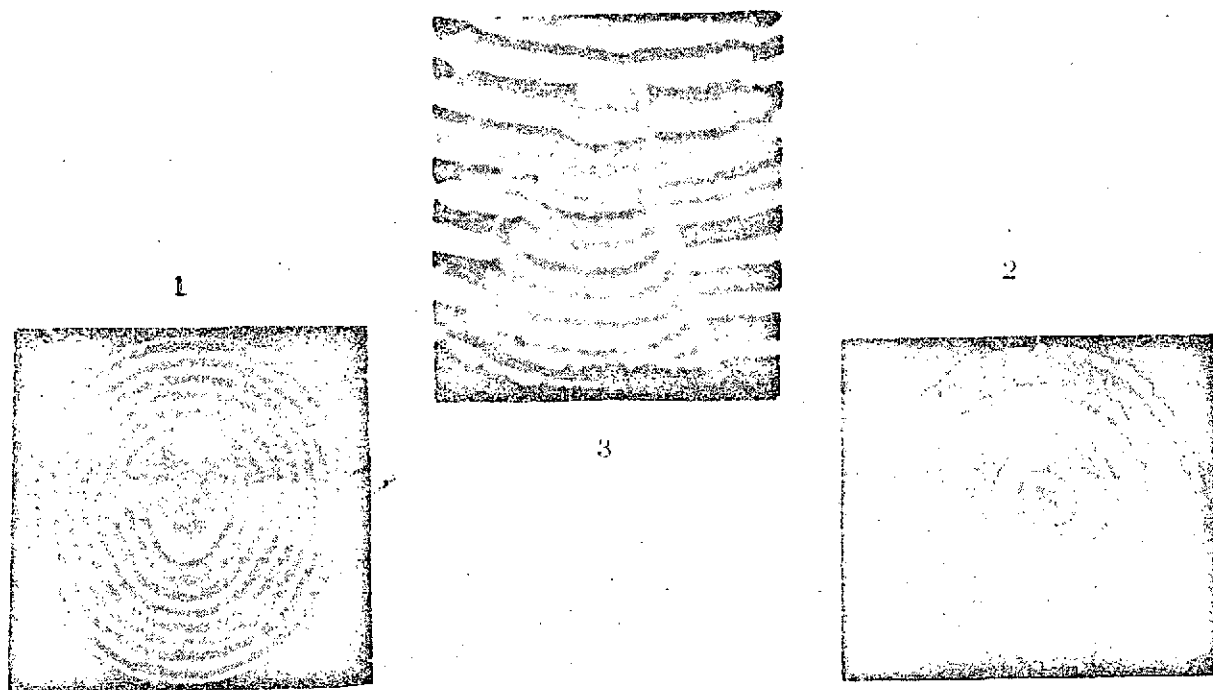Brand and Ye. Ye. Sel'kov).

Figure 8. Pushinskiy strain of aztinomyces with zone formation:
1--1 day; 2--3 day; 3--with a sector of arythmea.

However, the information available at the present time makes it
possible to recommend them for research both in space and on the
accelerator as a new object for studying the biophysics of strong
interaction and super-high energy hadrons as investigation of the

problem of the regulation of basic biological rhythm.

Membrane-Enzyme Complexes--Objects of Future Investigations

Multiple damage to cellular structure is characteristic of high and super-high energy hadrons as follows from the results of these investigations. It may be assumed that damage to massive cellular structures are most probable. In addition, the necessity of studying radiation damage to the most massive cellular structures also follows from a theoretical analysis of the results of experiments conducted with "ordinary" radiation sources, since an effective dose and the residual damage are determined by the total damage to all cellular structures in all systems of the organism [1, 9]. These problems are even more significant for hadron biology.

Membranes and membrane-enzyme complexes are the most massive cellular structures. Preservation of the structural and functional identity of these complexes is a necessary condition for normal cellular activity. The investigations conducted in our laboratory (Yu. A. Zaslavskiy) and an analysis of the available material show that ubiquinone has important significance in this regard, since it fulfills three functions on membranes: it is an element of the electron transportation, a powerful anti-oxident and a central component of the membrane for influencing its structural validity. Hence, investigations of the role of ubiquinone in radiation damage to mammals were begun [11]. The experiments conducted showed that in the case of the mammalian cells most resistant to radiation the cellular contents of ubiquinone was high. In the postradiation period, including after irradiating rats and guinea pigs in equally effective dosages, the rate of its increase and the level obtained were higher in rats resistant to radiation. No significant

changes took place in the ratio of the oxidized and reduced forms
of ubiquinone. The behavior of ubiquinone after irradiation is
typical for many compensatory-recovery reactions, the rapidity
and development of which influence the capacity of the organisms
to combat the development of radiation damage [1]. This led us to
assume that ubiquinone plays an important role both in the prevention
of radiation-oxidation damage to membrane lipids, and in recovery
processes on membranes, that is, in determining the radio-resistance
of the organisms [11].

On the other hand, investigations with high energy hadrons and
investigations in space showed that recovery processes are also
active in these conditions, and that radio protectors may be
effective. All that is presented above, makes it particularly
necessary to study the membrane-enzyme complexes and the radio
protective influence of ubiquinone as a possible special protector
for mass cellular strucutres, damage to which is assumed to be
characteristic during the action of high energy hadrons.

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